DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/22/2008 has been entered.

2. Claims 1, 3, 6, 16, 17, 18 and 19 have been amended.

3. Claim 20 has been newly added.

4. Claims 1-3, 6 and 16-20 are pending and are under examination.

5. This office action consists of new grounds of rejection.

Rejections Withdrawn

6. The rejection of claims 1-19 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of certain soluble ingredients from a microorganism as an adjuvant, does not reasonably provide enablement for the use of any soluble ingredient of a microorganism is withdraw in view of amendments to the claims.

7. The rejection of claim 4 under 35 U.S.C. 103(a) as being unpatentable over Ohno et al (CA/2362578 A1) and Ravindernath et al (U.S. Patent 6,218,166) is withdrawn in view of the cancellation of the claim.

Rejections Maintained

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10 Claims 1-3, 6 and 16-20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ohno et al (CA/2362578 A1; Publication Date: 08/17/2000) and Ravindernath et al (U.S. Patent 6,218,166; Date Issued: 04/17/2001). Please note that the above references are cited in the PTO-892 mailed 02/27/2007.

Applicants argue that the claims have been amended to more particularly recite the claimed invention, which combination is not suggested by the teachings of Ohno et al and Ravindernath et al (page 7 of the response filed 01/22/2008).

The above arguments are carefully considered but are not found persuasive. The applicants are reminded of the teachings of the prior art, wherein Ohno et al teach a tumor vaccine comprising of microparticles prepared from a solidified tumor material selected from a tumor tissue and/or tumor cell and a cytokine (Page 5, in particular), wherein the tumor material is chemically fixed using any fixing agent including formalin (Page 7, in particular) and contains as adjuvant, any substance that is known to be effective as an adjuvant including the bacterial derivatives, i.e. soluble ingredient from microorganisms (page 9, in particular) and Ravindernath et al teach immobilization of *Mycobaterium bovis* BCG obtained, soluble adjuvant into an intracellular compartment or to the outer membrane of an intact cell wherein the soluble adjuvant was immobilized

to intact cells (Summary of the invention; paragraphs 17, 22, 43 and 58, in particular). Thus, it is the examiners position that one of ordinary skill in the art at the time the invention was made would have been motivated to immobilize *Mycobaterium bovis* BCG derived, soluble adjuvant taught by Ravindernath et al to the formalin fixed tissue taught by Ohno et al with a reasonable expectation of success, because Ravindernath et al teach that incorporation of bacteria derived, soluble immunoadjuvant elicits immune responses against tumor antigens and prolongs survival and Ohno et al's invention taught that such solidified tumor material is easy to handle and is widely applicable.

Further, in view of *KSR International Co. v. Teleflex, Inc.*, 550 U.S._, 82, USPQ2d 1385 (2007) (please see pages 6-8 of the previous office action) it would have been *prima facie* obvious to modify the method of Ohno et al to produce tumor vaccine comprising tumor microparticles conjugated to soluble adjuvant obtained from *Mycobaterium bovis* BCG because Ohno specifically recognizes the problem of increasing the efficacy of tumor vaccines with adjuvants including bacterial derivatives and Ravindernath et al specifically teach that *Mycobaterium bovis* BCG obtained adjuvant is a known bacterial adjuvant which elicits immune responses against tumor antigens and prolongs survival (please see paragraph 58).

Furthermore, it would have been obvious to try the known methods of conjugation of bacterial adjuvants to conjugate an adjuvant obtained from *Mycobaterium bovis* BCG to the tumor microparticles for the making the claimed immunoconjugate with a reasonable expectation of success wherein the instantly

claimed invention is simple a predictable variant of the invention of Ohno et al in combination with Ravindemath et al, wherein the success of the solution to the problem would be a product of ordinary skill in the art.

Thus, since the conventional and successful techniques for conjugating bacterial adjuvants were known in the art at the time the invention was made and given the successful therapeutic efficacy of conjugation of BCG to a moiety that did not have defined tumor antigens, one of ordinary skill in the art would be motivated and would have a reasonable expectation of success to develop, in the interest of developing a more successful cancer therapy in human patients, an immunoconjugate as claimed with a variation of the technique of Ravindemath et al to conjugate the known adjuvant to the known microparticles for the treatment of tumor. Thus, a person of ordinary skill in the art, facing the wide range of needs created by the developments in the field of endeavor, would have seen a benefit to develop an immunoconjugate comprising a fragment, wherein said fragment is prepared from a chemically fixed tissue or cell washed to remove components not cross linked by chemical fixation, and wherein at least one soluble ingredient obtained from *Mycobacterium bovis* BCG is immobilized to the fragment.

New Grounds of Rejections

11. Claims 1, 3, 6 and 18-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The amendments filed on 01/22/2008 introduced NEW MATTER into claims 1, 3, 6 and 18-20. The claims recite “chemically fixed” which is not disclosed in the specification. The response filed on 01/22/2008 states that formalin, which is exemplified in the specification, is simply one example of a class of chemical tissue fixatives and provides support for "chemically fixed" (page 6 of the response filed 01/22/2008). By definition, and as admitted by the applicant, the term "chemically fixed" involves a broad range of chemical tissue fixatives such as Formaldehyde, Methanol, Ethanol, CDTA (cyclohexane diamine-tetraacetate), Na-Phosphate Buffer and Potassium Phosphate in addition to Formalin (please see Table 1 of Brinboim, U.S. Patent 5,976,829; Date Issued 11/02/1999). Thus, the claim includes a broad range of chemical fixatives that are not supported by the specification. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 (“Applicant should specifically point out the support for any amendments made to the disclosure.”) The specification as originally filed discloses formalin-fixation, does not apparently disclose any chemical fixative as broadly claimed. Applicants are required to specifically point our where the support for the newly added claim limitations can be found in the originally filed specification or claims or remove the limitation from the claim.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
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/David J Blanchard/
Primary Examiner, Art Unit 1643